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3 **Supplementary information**

4 **Table S1.** *F. psychrophilum* ancestral and phage-resistant isolates used in this study

Strain	Phage used for selection	Reference	Accession number
950106-1/1	-	(1)	CP008902
V1-20	FpV4	Christiansen et al. Unpublished	CP008879
V2-20	FpV21	Christiansen et al. Unpublished	CP008880
V3-5	FpV4	Christiansen et al. Unpublished	CP008878
V4-24	Cocktail 11 different phages*	Christiansen et al. Unpublished	CP008881
V4-28	Cocktail 11 different phages*	Christiansen et al. Unpublished	CP008882
V4-33	FpV21	Christiansen et al. Unpublished	CP008883

5 * Cockatil consisting of 11 phages Fpv1, Fpv2, Fpv3, Fpv4, Fpv9, Fpv13, Fpv15, Fpv17, Fpv19,
6 Fpv21 and Fpv22 previously described by Stenholm, et al. (1)

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12 **Table S2. Bacteriophages used in this study**

Bacteriophage	Site origin	Isolation strain	Year	Phage family	Genome size (kbp)	Reference
1H	Chile. Los Lagos	MH1	2008	<i>Siphoviridae</i>	50	(2)
6H	Chile. Los Lagos	MH1	2008	<i>Siphoviridae</i>	50	(2)
2P	Chile. X región	PG2	2009	<i>Siphoviridae</i>	50	(2)
23T	Chile. Santiago	T23	2009	<i>Siphoviridae</i>	50	(2)
2A	Chile. Los Ángeles	A2	2009	<i>Podoviridae</i>	50	(2)
P1	Chile. Puerto Montt	PL1R2	2011	ND	ND	(2)
P2	Chile. Puerto Montt	PL1R2	2011	ND	ND	(3)
P3	Chile. Puerto Montt	PL1R2	2011	ND	ND	(3)
P4	Chile. Puerto Montt	PL1R2	2011	ND	ND	(3)
P5	Chile. Puerto Montt	PL1R2	2011	ND	ND	(3)
Fpv1	Denmark. Fish Farm C	950106-1/1	2005	ND	90	(1)
Fpv2	Denmark. Fish Farm C	950106-1/1	2005	<i>Podoviridae</i>	90	(1)
Fpv3	Denmark. Fish Farm K	950106-1/1	2005	ND	90	(1)
Fpv4	Denmark. Fish Farm L	950106-1/1	2005	<i>Podoviridae</i>	90	(1)
Fpv5	Denmark. Fish Farm E	950106-1/1	2005	ND	48	(1)
Fpv6	Denmark. Fish Farm E	950106-1/1	2005	ND	48	(1)
Fpv7	Denmark. Fish Farm E	950106-1/1	2005	<i>Siphoviridae</i>	48	(1)
Fpv8	Denmark. Fish Farm E	950106-1/1	2005	ND	48	(1)
Fpv9	Denmark. Fish Farm F	950106-1/1	2005	<i>Siphoviridae</i>	48	(1)
Fpv10	Denmark. Fish Farm H	950106-1/1	2005	<i>Siphoviridae</i>	48	(1)
Fpv11	Denmark. Fish Farm H	950106-1/1	2005	ND	48	(1)
Fpv12	Denmark. Fish Farm F	Mixture*	2005	ND	12	(1)
Fpv13	Denmark. Fish	Mixture*	2005	ND	12	(1)

	Farm F					
Fpv14	Denmark. Fish Farm I	950106-1/1	2005	<i>Siphoviridae</i>	12	(1)
Fpv15	Denmark. Fish Farm I	950106-1/1	2005	ND	12	(1)
Fpv16	Denmark. Fish Farm O	Mixture ^a	2005	ND	12	(1)
Fpv17	Denmark. Fish Farm O	Mixture ^a	2005	ND	12	(1)
Fpv18	Denmark. Fish Farm P	Mixture ^a	2005	ND	10	(1)
Fpv19	Denmark. Fish Farm L	950106-1/1	2005	ND	8	(1)
Fpv20	Denmark. Fish Farm L	950106-1/1	2005	ND	ND	(1)
Fpv21	Denmark. Fish Farm L	950106-1/1	2005	ND	ND	(1)
Fpv22	Denmark. Fish Farm O	Mixture*	2005	ND	ND	(1)

13 **ND: not determined**

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20 **Table S3.** Genes with mutations in *F. psychrophilum* phage-resistant isolates

Gene accession	Type of mutation	Phage-resistant isolates	Function	^a Cellular localization	^b TMH/SP	^c Effect mutation
WP_0119 62354.1- WP_0119 62360.1	Deletions/insertions	All	Probable cell surface protein (leucine rich repeat proteins in tandem)	CyM	-/+	I/R
WP_0119 64261.1	Deletion	All	Two-component system response regulatory protein, LytTR family	CyM	-/-	D
WP_0163 61986.1	Deletion	V1-20;V4-24; V4-28;V4-33	Putative adhesin	CyM	+/+	SC
WP_0119 62492.1	Deletion	V1-20;V4-24; V4-28;V4-33	Probable outer membrane protein precursor OmpA family	CyM	+/+	D
WP_0119 63051.1	Insertion	V1-20;V3-5	50S ribosomal protein L20	Cy	-/-	FS
WP_0119 62491.1	Deletion	V1-20;V4-24; V4-28;V4-33	Hypothetical protein precursor	Cy	-/-	D
WP_0119 63061.1	Deletion	All	Threonine-tRNA ligase	Cy	-/-	FS
WP_0119 63567.1	Insertion	V4-33	Phytoene dehydrogenase	Cy	-/-	SC
WP_0119 64125.1	Insertion	V1-20	Riboflavin biosynthesis protein RibD	Cy	-/-	SC
WP_0119 64316.1	Deletion	All	NADH dehydrogenase I, F subunit	Cy	-/-	FS
WP_0119 64122.1	Insertion	V1-20	ABC-type transport system, permease component	CyM	-/-	AC
<u>WP_0119</u> <u>64239.1</u>	Deletion	V2-20	Major facilitator superfamily (MFS) permease	CyM	+/-	D
WP_0119 64253.1	Deletion	V2-20; V4-24	Putative transporter	Uk	-/-	D

WP_0119 63428.1	Deletion	V4-33	UDP-N-acetyl-D-galactosamine dehydrogenase	Cy	-/-	SC
WP_0119 63518.1	Deletion	V2-20	UDP-N-acetylmuramoyl-tripeptide-D-alanyl-D-alanine ligase	Cy	-/-	D
WP_0119 63517.1	Deletion	V2-20	Gliding motility lipoprotein GldJ	Uk	-/+	FS
WP_0119 64073.1	Insertion	V4-24	Gliding motility protein GldM	Uk	+/+	SC
WP_0119 64075.1	Deletion	V1-20	Gliding motility protein GldK	Uk	-/+	SC
-	Insertion	V2-20	Truncated collagenase precursor, C-terminal region	Uk	-/-	-
WP_0119 64246.1	Insertion	V4-28	Probable type II restriction endonuclease	Cy	-/-	AC
WP_0163 61990.1	Deletion	V1-20; V3-5; V4-24; V4-28	Transposase mutator type	Cy	-/-	D
WP_0119 63984.1	Deletions and insertions	V3-5; V4-28;	Hypothetical protein	Uk	-/-	I
WP_0119 64255.1	Insertion	V4-33	Hypothetical protein	Uk	-/-	SC
-	Deletion	V1-20; V3-5	Pseudo protein	Uk	-/-	D
WP_0119 64240.1	Deletion	V1-20	Hypothetical protein	Cy	-/-	D
WP_0119 64241.1	Deletion	V3-5	Hypothetical protein	Uk	+/-	D
	Deletion	V1-20; V3-5	Hypothetical protein	Uk	-/-	D
WP_0119 64258.1	Deletion	All	Hypothetical protein	CyM	+/-	D
WP_0119 64259.1	Deletion	All	Hypothetical protein	Uk	-/-	D

WP_011964260.1	Deletion	All	Hypothetical protein	Cy	-/-	D
WP_011963641.1	Insertion	V3-5	Protein of unknown function	Cy	-/-	FS
WP_011963641.1	Insertion	V3-5	Protein of unknown function	Cy	-/-	SC
WP_011964255.1	Insertion	All	Protein of unknown function	CyM	+/-	SC
WP_011962979.1	Deletion	V4-24; V4-28; V4-33	Protein of unknown function	CyM	+/-	D
WP_011963238.1	Deletion	All	Protein of unknown function	Cy	-/+	SC
WP_011964251.1	Insertion	V4-24	Protein of unknown function putative pseudogene C-terminal region	-	-	-
WP_011964252.1	Insertion	V4-24	Protein of unknown function putative pseudogene N-terminal region	-	-	-
WP_011964254.1	Deletion	V2-20;V4-24	Protein unknown function	Uk	-/-	D
-	Deletion	All	Prophage type-6H	-	-	D
WP_011962309.1	Point	V3-5;V4-28	BatB protein	Cy	+/-	FS
WP_011963158.1	Point	V4-33	Probable short-chain type dehydrogenase	Cy	-/+	AC
WP_011963925.1	Point	V3-5	Probable ATP-dependent RNA helicase, DEAD/DEAH box family	Cy	-/-	AC
WP_011964545.1	Point	V4-33	ATP synthase alpha subunit	Cy	-/-	AC
WP_011963121.1	Point	V1-20	Probable UDP-N-acetylglucosamine acyltransferase	Cy	-/-	AC
WP_011963517.1	Point	V4-33	Gliding motility lipoprotein Gldj	Uk	-/+	SC

WP_0119 62997.1	Point	V2-20;V3-5;V4- 24;V4-33	Putative transcriptional regulator XRE family	Cy	-/-	AC
WP_0119 64292.1	Point	V3-5	Probable phage protein	Uk	-/-	AC
WP_0119 64292.1	Point	V3-5	Probable phage protein	Uk	-/-	^d AC
WP_0163 61981.1	Point	V3-5	Hypothetical protein	Uk	-/-	^d AC
WP_0163 61981.1	Point	V3-5	Hypothetical protein	Uk	-/-	^d AC
WP_0163 61981.1	Point	V3-5	Hypothetical protein	Uk	-/-	^d AC
WP_0163 61981.1	Point	V3-5	Hypothetical protein	Uk	-/-	^d AC
WP_0119 63673.1	Point	V1-20	Protein of unknown function	Cy	-/-	AC
WP_0119 63960.1	Point	V3-5	Protein of unknown function Yfkh	CyM	+/-	AC
WP_0119 63961.1	Point	V3-5	Protein of unknown function	Cy	-/-	AC
WP_0119 63238.1	Point	V1-20	Protein of unknown function	CyM	+/+	AC
WP_0119 64248.1	Point	V1-20; V3- 5;V4-24; V4-33	Protein of unknown function	CyM	+/+	AC

21 ^aCellular localization: Cytoplasmic (Cy); Cytoplasmic membrane (CyM); Unknown (Uk).

22 ^bTHM/SP: Transmembrane helice/Signal peptide.

23 ^cEffect mutation: amino acid change (AC); frameshift (FS); stop codon (SC); Indels/

24 rearrangements (I/R); Deletion full gene (D).

25 ^dAC: mutation caused aminoacid change but the gene also presented a deletion.

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30 Table S4. Elastinase activity in ancestral strain 950106-1/1 and the six phage resistant isolates

Strain	Elastinase activity
950106-1/1	+++
V1-20	-
V2-20	-
V3-5	++
V4-24	-
V4-28	-
V4-33	-

31 +++ “presence of elastinase activity”

32 ++ “reduced presence of elastinase activity”

33 - “absence of elastinase activity”

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35 References:

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 41 protection against bacterial cold water disease in salmonids. J. Fish Dis. **35**:193-201.

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